UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address : COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/340,664	11/16/94	GAUTVIK K	FORSKG.0001

SPECTOR, EXAMINER

18N2/0908

LERNER DAVID LITTENBERG
KRUMHOLZ & MENTLIK
600 SOUTH AVENUE WEST
WESTFIELD NJ 07090

ART UNIT	PAPER NUMBER
1812	8

DATE MAILED: 09/08/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/8/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-20 are pending in the application.
   Of the above, claims 6-10, 12, 14, 16-20 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-5, 11, 13, 15 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1-20 were ~~are~~ subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

340664.1

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Part III: Detailed Office Action

Restriction Requirement:

Applicant's election with traverse of Invention I, claims 1-5, 11, 13 and 15 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the examination of Inventions I and II would not constitute a burden to search. This is not found persuasive because contrary to applicants' assertion that any search of the prior art in regard to group I will reveal whether any prior art exists as to Group II, a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. For Example, Invention II requires search of KEX protease cleavage, and the art surrounding mutagenesis to remove such cleavage sites.

The requirement is still deemed proper and is therefore made FINAL.

Formal Matters:

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required: there is no antecedent basis in the specification for the recitation of 90% or 95% purity of the claimed protein.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because of the following informalities; Appropriate correction is required for each of the following items:

The status of all applications to which reference is made in the first paragraph of the specification should be updated.

The information at page 1, lines 20-23 appears duplicative of the first paragraph of the

same page.

The brief description of the drawings should reflect each individual panel of each figure. For Example, the description of Figure 8 should begin "Figures 8A-8C show..." or the equivalent. This objection applies to the descriptions of Figures 8, 9 and 13.

With further respect to Figure 9, it is noted that while the description of the figure refers to panels A-E, only four panels are seen in the Figure, and only one of the four (B) is labelled. Correction is required.

Figure 10 is objected to because the quality of the submitted photocopy is poor. Applicants are required to substitute a "clean" copy of the Figure.

Figures 6 and 7, as submitted contained information placed too far to the top of the page, such that information was lost when holes were punched in the figures for insertion into the file wrapper by the Patent Office. Applicants should submit substitute copies of these figures, making sure that all information is sufficiently distant from the top of the page (allow at least one inch).

Double Patenting Rejections:

Claims 1-5, 11, 13 and 15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 5,010,010. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the protein claimed in the patent appears to be physically and functionally identical to the protein claimed in the pending claims, the instant claims are not restricted to protein which has been recombinantly produced in yeast cells. Although the patented claim is silent with respect to how pure the protein was, the protein is deemed to meet the purity limitations of the pending claims, alternatively it would have been obvious to purify the protein of the patented claim, using routine protein purification methodology, to be used for its known and expected properties.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification does not enable how to make hPTH by "synthetic" means. The entire specification is directed to the recombinant production of hPTH in microbial cells (bacteria or yeast), and contains no description of how to make the peptide synthetically. In the absence of any such description, the Examiner cannot determine whether "synthetic" hPTH refers to hPTH which has been made via chemical synthesis and has the naturally occurring amino acid sequence, or alternatively, may refer to a structurally distinct molecule which has PTH activity. In the absence of any guidance as to what comprises "synthetic hPTH", it would require undue experimentation to make and use such.

Claim 2 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-5, 11, 13 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 are indefinite as it is not clear what the metes and bounds of "essentially pure" and "substantially pure" are, and further, how such differ; it is noted that if the terms are equivalent, then claims 1 and 3 are duplicative.

Claims 11 and 13 are indefinite because, if claim 11 is intended as a product by process claim it does not include sufficient steps to achieve the stated result, namely there is no purification or isolation step. Alternatively, it is not clear how claim 13 further limits claim 11, as purification or isolation would seem to be implicit in claim 11.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is rejected under 35 U.S.C. § 102(b) as being anticipated by Kumagaye et al (J. Chrom. 327:327) or Kimura et al. (BBRC 114:493) or Fairwell et al. (Biochem. 22:2691).

Kumagaye et al. disclose the separation via cation exchange HPLC of two 84 amino acid forms of hPTH, Asn_{76} and Asp_{76}. The peptides were made synthetically (see end of first page), and were substantially pure, in view of the fact that separation of two such closely related species was possible.

Kimura et al. disclose the synthesis of Asn_{76} hPTH, which was purified and confirmed as being homogeneous on the basis of HPLC and peptide mapping (see abstract, and page 498 "We concluded that our present product was reasonably homogeneous").

Fairwell et al. disclose solid phase synthesis, purification and characterization of hPTH (1-84) (see title, abstract). The protein appears to have been at least 95% pure on the basis of minimal (5-6%) residue preview on sequencing and biological activity (see page 2694).

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-5, 11, 13 and 15 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Brewer et al., U.S. Patent Number 3,886,132.

Brewer et al. disclose highly purified human PTH. See abstract, and col. 2 lines 49-60 wherein it is disclosed that the preparation was pure enough to sequence 34 amino acid residues starting at the amino terminus of the protein. Thus, the protein as purified by Brewer et al. appears to be consistent with the limitations of the instant claims with respect to being pure hPTH. It cannot be determined by the Examiner whether Brewer's protein specifically meets the limitations of being 90% or 95% pure, although it would seem likely that it did, given Brewer's ability to sequence 34 residues. It is noted that the only portion of the specification which relates to purity is the disclosure that the protein was partially sequenced (page 7, starting at line 27),

which the ordinary artisan would recognize as requiring a relatively pure preparation of the desired protein (although no exact percentage purity can be implied). Based upon the fact that the specification discloses obtaining the sequence of 19 and 45 amino acids respectively, from the yeast and E. coli-produced protein, Brewer's ability to obtain 34 amino acids would seem to indicate that comparable purity was achieved. In the event Brewer's protein was less than 90% or 95% pure, it would have been obvious to further purify Brewer's protein using routine protein purification methodology, and one of ordinary skill in the art would have been motivated to do so in view of the known pharmacological uses of the protein, and the art-recognized advantages of using the purest protein preparation possible for pharmaceutical use.

Although Claims 1-5 are not drafted in product-by-process format, the recitation of "recombinant" and "synthetic" is suggestive of such, and claims 11, 13 and 15 are at least loosely in product by process format. The decisional law has clearly emphasized that such claims are directed to a product and are not restrictive to a process because they are not construed as being limited to the product of a specific process (*In re Bridgeford*, 149 USPQ 55: *In re Hirao*, 190 USPQ 15). Patentability depends on whether the product is known in the art or obvious, and is not governed by its process of production (*In re Klug*, 142 USPQ 161); therefore, the burden is upon applicants to establish a patentable difference between the claimed product and that of the prior art (*In re Fessman*, 180 USPQ 324). Further held was that when a prior art product reasonably appears to be the same as that claimed, but differs by the process via which it was produced, a rejection of this nature is eminently fair and the burden is upon applicants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685; *In re Marosi*, 218 USPQ 289; *In re Thorpe*, 227 USPQ 965; *In re Fitzgerald*, 205 USPQ 594; and as more recently emphasized in *Ex parte Gray*, 10 USPQ 2d 1922; *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 9 USPQ 2d 1833; and *Scripps Clinic v. Genentech Inc.*, 3 USPQ 2d 1481). In view of the fact that the courts have clearly emphasized that product-by-process (p-b-p) claims are not patentable over product claims unless there has been established a patentable difference, one having ordinary skill in the art at the time of the invention would have expected that the hPTH produced by

organic synthesis or by the recombinant process disclosed in the instant specification would be functionally/biologically equivalent to native hPTH as purified by Brewer et al. and would therefore function in a manner taught by the prior art, thus rendering applicant's claims prima facie obvious in the event that the claim is not anticipated by the prior art.

Claims 1, 2, 4, 5, 11, 13 and 15 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Kumagaye et al (J. Chrom. 327:327) or Kimura et al. (BBRC 114:493) or Fairwell et al. (Biochem. 22:2691). The three references all disclose hPTH which was synthetically made and purified to at least 95% purity; the teachings of each are outlined in the above rejection of claim 3 under 35 U.S.C. §102(b). The claims differ from the cited references only in that the claims are product-by-process claims, in which a different process than those used in the cited prior art is used. In the absence of evidence to the contrary, the claimed protein itself appears to be anticipated by the prior art, or alternatively is considered to be *prima facie* obvious over the prior art proteins, for reasons cited in the preceding paragraph.

Advisory Information:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Niall et al. (PNAS 71:384) and Keutmann et al. (Biochem. 13:1646) disclose highly purified preparations of human PTH.

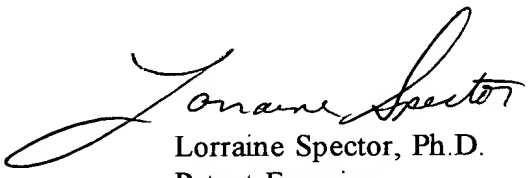
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Garnette D. Draper, can be reached at (703)308-4232.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The Art Unit 1812 Fax Center number is (703) 308-0294. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the Examiner at the telephone number above when a fax is being transmitted.



Lorraine Spector, Ph.D.
Patent Examiner

LMS
340664.1
8/31/95